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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,598	09/20/1999	MASAHICO MIHARA	350292000800	4167
25225	7590	07/25/2005		
MORRISON & FOERSTER LLP 3811 VALLEY CENTRE DRIVE SUITE 500 SAN DIEGO, CA 92130-2332			EXAMINER MURPHY, JOSEPH F	
			ART UNIT 1646	PAPER NUMBER
DATE MAILED: 07/25/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/381,598	<b>Applicant(s)</b> MIHARA, MASAHIKO	
	<b>Examiner</b> Joseph F. Murphy	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2005.  
 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 14-22 and 33-38 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 14-22, 33-38 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
     \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>06132005</u> . | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Formal Matters***

Claims 14-22, 33-38 are pending and under consideration.

### ***Response to Arguments***

The Declaration under 37 CFR 1.132 filed 6/13/2005 is sufficient to overcome the rejection of claims 14-22, 33 based upon 35 USC 112 first paragraph.

Applicant's arguments filed 6/13/2005 with regard to the rejection under 35 USC 103 (a) have been fully considered but they are not persuasive for the reasons set forth below.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14-22, 33-38 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gijbels et al (1995) in view of Vink et al. (1990), and further in view of U.S. Patent No. 5,605,930 (Samid) for reasons of record set forth in the Office Action of 3/11/2003 and 11/01/2004.

The rejection of record set forth that Gijbels et al. teaches the administration of antibodies to IL-6 in the EAE model of multiple sclerosis (page 799, Table I). The administration of the mAB to IL-6 significantly reduced the development of EAE, both in actively induced EAE and in the adoptive transfer model of EAE. Gijbels does not disclose administration of antibodies to IL-6 receptor. Vink et al. teaches the administration of anti-IL-6 receptor antibodies (page 998,

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second column, third paragraph) as well as antibodies to IL-6 (page 998, Figure 1). These antibodies both block the action of IL-6 (page 998, column 2, third paragraph). Given the teaching of Gijbels of the beneficial effect of blocking the effect of IL-6 in the EAE model, along with the teaching of Vink that the effect of IL-6 can be neutralized by antibodies to both IL-6 and IL-6 receptor, it would have been obvious to one of skill in the art at the time the invention was made to practice a method of administration of anti-IL-6 receptor antibodies to treat MS. The motivation is provided by Gijbels who concludes that the protective effect of anti-IL-6 in EAE might have therapeutic effect in inflammatory conditions of the CNS, including MS (page 804), and that given the disclosure of Samid of the central role that IL-6 plays in inflammatory processes, it would be an expected property of the method of administration of anti-IL-6 receptor antibodies to treat MS, that this method of administration would treat other autoimmune and inflammatory processes, such as uveitis, thyroiditis, dermatitis and hypersensitivity.

Applicant argues that the cited combination fails to render the claimed methods *prima facie* obvious in view of the entirety of the cited documents. Applicant argues that the cited combination fails to teach or suggest the claimed methods, because Gijbels complete teaching regarding IL-6 activity after anti-IL-6 antibody administration fails to predict the exact mechanism of action for the observed clinical effects, and that when read in its entirety, Gijbels lacks any prediction as to how the anti-IL-6 antibody functioned. However, an examination of the Gijbels reference demonstrates that the reference teaches the function of the mAB administered had an anti IL-6 activity, specifically, the Gijbels reference teaches the use of neutralizing mAB to IL-6 to examine the role of IL-6 in the pathogenesis of EAE and to evaluate the potential use of anti-IL-6 therapy in inflammatory CNS disorders (page 796, column 1,

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second paragraph). Gijbels further teaches that they administered neutralizing mAB to IL-6 to animals in which EAE was induced and that administration of the mAB significantly reduced the development of EAE (page 800, column 2, second paragraph). Thus, the mAB of Gijbels is taught in the reference as neutralizing IL-6 activity. Applicant further argues that neither Vink nor Samid remedy this deficiency because Vink discloses the use of antibodies targeting IL-6 and its receptor in B cells and that T cells or associated diseases are not mentioned in Vink. Likewise, Samid is completely silent regarding the use of an anti-IL-6 receptor antibody to treat T-cell mediated diseases. However, the Gijbels reference teaches that use of mAB to neutralize IL-6 activity, and the Vink reference was cited to demonstrate that it was known in the art that IL-6 activity can be neutralized by antibodies to either IL-6 or the IL-6 receptor (page 998, second column, third paragraph and Figure 1), and this teaching is not dependent of the model system, because the Gijbels reference supplies the teaching of the neutralization of IL-6 in a T-cell mediated disease (the EAE model of MS) system. The Samid reference was cited to establish the central role that IL-6 plays in inflammatory processes, and that it would be an expected property of the method of administration of anti-IL-6 receptor antibodies to treat MS, that this method of administration would treat other autoimmune and inflammatory processes, such as uveitis, thyroiditis, dermatitis and hypersensitivity.

Applicant further argues that the cited combination fails to provide a motivation to combine the references. The motivation to combine set forth by the Examiner relies on incomplete consideration of the cited references and a misunderstanding of the art, because there is nothing in Gijbels that teaches or suggests that predicts an anti-IL-6 receptor antibody would have a similar effect. However, the Gijbels reference clearly teaches that the effects of the mAB

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administered is to neutralize IL-6 activity (page 800, column 2, second paragraph), and the Vink reference shows that antibodies to IL-6 and IL-6 receptor have similar effects when administered, by blocking IL-6 activity, while the Gijbels reference teaches the efficacy of anti-IL-6 activity therapy in the EAE model of MS.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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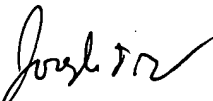
***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.  
Primary Examiner  
Art Unit 1646  
July 18, 2005

  
**JOSEPH MURPHY**  
**PATENT EXAMINER**